REMARKS

Claims 1-17 are pending in the current application. In an office action dated October 28, 2008 ("Office Action"), the Examiner rejected claims 1, 5-9, and 15 under 35 U.S.C. §102(b) as being anticipated by Bergeron et al., U.S. Patent No. 5,773,027 ("Bergeron"), rejected claims 1-5, 7-9, and 15-17 under 35 U.S.C. §103(a) as being unpatentable over Kirpotin, U.S. Patent No. 6,110,491 ("Kirpotin"), rejected claim 6 under 35 U.S.C. §103(a) as being unpatentable over Kirpotin in view of Thibodeau, Molecular Engineering, 1991, 275-293 ("Thibodeau") and Konigsberg et al., U.S. Patent No. 5,258,499 ("Konigsberg"), and rejected claims 1-9 and 15-17 under 35 U.S.C. §103(a) as being unpatentable over Bergeron in view of Kirpotin. Applicants' representative has amended independent claim 1 to more distinctly claim and particularly point out that which Applicants regard as their invention. Support for this amendment can be found in the paragraph beginning on line 24 of page 15 of the current application. As a result of the amendment, Applicants' representative believes that many of the Examiner's rejections no longer apply, and traverses those portions of the Examiner's rejections that may still apply, below.

Applicants' representative notes that, in the rejection of claims 1, 5-9, and 15 being anticipated by Bergeron, on page 3 of the Office Action, the Examiner states:

> The reference teaches the intravenous administration of liposomes to rats (Table 3). Thus, the lipid-drug complexes are suitable for subcutaneous administration.

Applicants' representative does not understand this statement. Intravenous administration is different from subcutaneous administration, and it is well-known that many drugs are suitable for one of these methods for introduction into an organism but not for the other. When a drug can be delivered by either method, the protocol, concentrations, carrier solutions, and other parameters may be quite different in the two cases. The Examiner provides no support for assuming that a drug that can be intravenously administered is necessarily suitable for subcutaneous administration. In Applicants' representative's

respectfully offered opinion, this assertion is unsupported and unsupportable.

Kirpotin employs a method of preparing compound-loaded liposomes that includes compound loading by pH precipitation, as discussed beginning on line 44 of column 10. In this technique, a drug is prepared in solution at a first pH at which the drug is water soluble, and is then added to a liposome dispersion, in which the liposomes' internal pH, or second pH, is different from the first pH. The drug is poorly soluble at the second pH. When the drug diffuses into the liposomes, its solubility decreases to the point that the drug precipitates out of solution within the liposomes. This is a different approach than that used to prepare the currently claimed lipid-drug complex. A drug that is precipitated within a liposome has different chemical characteristics than a drug which is incorporated into a lipid-drug complex at neutral pH. There is no reason to suspect or speculate that Kirpotin's compound-loaded liposomes would necessarily release the precipitated drug when the pH of the solution containing the liposomes is lowered to between pH 5.0 and pH 5.5.

Bergeron prepares liposomes that encapsulate antiviral drugs in solution by adding the drug to a flask containing a thin lipid film. Again, this technique also, like that of Kirpotin, differs substantially from the technique used to prepare the currently claimed lipid-drug complex.

Liposomes that encapsulate antiviral drugs, as prepared by Bergeron, are not stoichiometric molecular compounds and cannot be assumed to be equivalent in molecular weight, structure, concentrations of solutes within the solution contained in the liposomes, or in any other parameter or characteristic to those prepared according to Kirpotin's method or those prepared according to the methods of the present invention. Liposomes are complex, non-stoichiometric, molecular complexes that may contain many thousands to millions of lipid molecules and millions to billions of small-molecule compounds and solvent molecules. Depending on the conditions in which lipid-drug complexes are manufactured, an enormous number of different types of liposomes or other complexes can be formed, each type having substantially different physical properties from other types of liposomes. The currently claimed lipid-drug complex is prepared in a way that lipid-soluble drugs having low water solubility at neutral pH are

efficiently incorporated with high efficiency into the lipid-drug complex. Lipid-drug complexes prepared according to the present invention have the useful property that, at low pH, which may occur in the micro-environmental vicinity of virally infected cells or tumor cells, the drug dissociates with high efficiency from the lipid-drug complex. The Examiner states, on page 5 of the Office Action:

> The reference do not explicitly teach that the drug substantially dissociates from a lipid-drug complex within a pH range of 5.0 – 8.0.

This property of drug dissociation at lower-than-neutral pH is not taught or suggested as being associated with the various liposome-based formulations disclosed in the cited references, and there is absolutely no basis for concluding that this property is inherent in those formulations, particularly when it would be impossible for the Examiner, and quite difficult or impossible for anyone else, to be able to state exactly what are the structures and chemical compositions of the liposome-based formulations produced by the methods disclosed in the cited references.

On page 5 of the Office Action, the Examiner states:

> Kirpotin teach the components of the lipid-drug complex, the drug indinaver can be entrapped in a liposome and hence it would be obvious to one of ordinary skill in the art that the drug substantially dissociates form the drug complex within a pH range from about 5- 8.

The Examiner provides no support for this speculative and unsubstantiated conclusion. As noted above, this conclusion cannot be supported scientifically from the cited references or from scientific principles. As those ordinarily skilled in the art well realize, a liposome comprise a lipid bilayer that is not water soluble and that sequesters a solution within the liposome from contact and chemical communication with the solution external to the liposome. It would not be obvious to one of ordinary skill in the art, or even to an undergraduate major in biochemistry, that a precipitated drug complex within a liposome would be expelled from a liposome when the solution in which the liposome is contained is modified to have a pH in a range from about 5.0 to 8.0. While the Examiner claims such disassociation is an inherent property of Kirpotin's formulation, there is no basis in chemistry, biochemistry, or any other chemically related field to support this conclusion.

The Examiner repeats this unsupported and incorrect conclusion on page 8 of the Office Action. Furthermore, claim 4, as originally filed, erroneously included the upper pH of 8.0 in the range of pHs at which dissociation occurs, when, in fact, the upper pH should be 5.5, as stated in the above-referenced portion of the current application. The Examiner has therefore claimed, as inherent to Kirpotin's compound-loaded liposomes, a property that is not associated with the currently-claimed lipid-drug complex and that is very likely not an inherent characteristic of any of the liposomes disclosed in the cited references.

The currently-claimed lipid-drug complex is prepared by methods of the present invention to have the property that the drug dissociates from the lipid-drug complex at relatively low pH, below pH 5.5. The cited references to not teach, mention, or suggest the low-pH drug-dissociation characteristic of the currently claimed lipid-drug complex, and, because the compound-loaded liposomes of the cited references are prepared by quite different procedures, and therefore likely to substantially differ in chemical composition, structure, and physical characteristics from the currently claimed lipid-drug complex, there is no basis for considering the low-pH drug-dissociation characteristic of the currently claimed lipid-drug complex to inherent in the compound-loaded liposomes of the cited references.

In Applicants' representative's opinion, all of the claims remaining in the current application are clearly allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,
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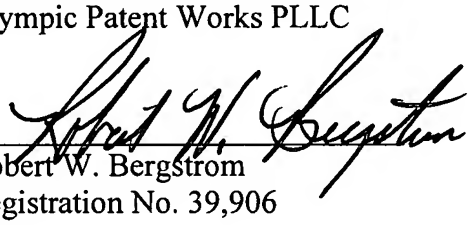

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